

U.S.S.N. 10/698,289

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In the Claims:

Please amend the claims as set forth in the following Listing of the Claims.

LISTING OF THE CLAIMS

- 1.(Original) A system for detecting an analyte, the system comprising:
 - a sensor adapted to detect the analyte, the sensor comprising a polymer matrix, a fluorophore and a membrane surrounding the matrix;
 - an excitation source to excite the fluorophore;
 - a first detector adapted to detect light of a first wavelength emitted by the sensor;
 - a second detector adapted to detect light of a second wavelength emitted by the sensor; and
 - a processor for processing signals from the first and second detectors corresponding to light detected at the first and second detectors.
- 2.(Currently Amended) The system of claim [1] 30, wherein the excitation source is adapted to transcutaneously excite the fluorophore.
- 3.(Currently Amended) The system of claim [1] 30, wherein the first detector and the second detector are [is] adapted to transcutaneously detect light emitted by the sensor.
- 4.(Currently Amended) The system of claim [1] 30, further comprising a telemetry system for transmitting a signal corresponding to light detected at the first and second detectors to a remote location.
- 5.(Currently Amended) The system of claim [1] 30, further comprising a first filter to filter light received by the first detector.
- 6.(Original) The system of claim 5, further comprising a second filter to filter light received by the second detector.

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7.(Currently Amended) The system of claim [1] 30, further comprising a first dichromatic mirror positioned to reflect light emitted by the excitation source and to transmit light emitted by the sensor.

8.(Original) The system of claim 7, further comprising a second dichromatic mirror positioned to reflect a first wavelength of light emitted by the sensor and to transmit a second wavelength of light emitted by the sensor.

9.(Currently Amended) The system of claim [1] 30, further comprising a fiber optic operatively connected to the excitation source.

10.(Original) The system of claim 9, wherein the fiber optic comprises a single mode optical fiber.

11.(Currently Amended) The system of claim [1] 30, further comprising a fiber optic operatively coupled to at least one of the detectors and adapted to transmit light from the sensor to the at least one detector.

12.(Currently Amended) The system of claim [1] 30, further comprising a pump adapted to receive an instruction from the processor and to deliver an amount of a medicament, in response to the instruction.

13.(Currently Amended) The system of claim [1] 30, wherein the fluorophores are mobile within the matrix.

14.(Currently Amended) The system of claim [1] 30, wherein the processor is adapted to store a value corresponding to a property of the detected analyte as a function of time.

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15.(Currently Amended) The system of claim [1] 30, wherein the processor is adapted to transfer a value corresponding to a property of the detected analyte to a remote device.

16. (Currently Amended) The system of claim [1] 30, wherein the processor is adapted to relate signals corresponding to the light detected by the first and second detectors to a property of the analyte.

17.(Original) The system of claim 16, wherein the property comprises the concentration of the analyte.

18.(Currently Amended) The system of claim [1] 30, wherein the processor is adapted to provide instructions regarding an activity related to a property of the detected analyte.

19.(Currently Amended) The system of claim [1] 30, wherein the processor is adapted to provide instructions related to a property of the detected analyte to at least one of a mammal and a device.

20.(Original) The system of claim 19, wherein the instructions comprise instructions to administer least one of insulin, glucose or a combination thereof.

21.(Currently Amended) The system of claim [1] 30, wherein the processor is adapted to provide an alarm when a predetermined condition related to a property of the analyte is met.

22.(Currently Amended) The system of claim [1] 30, wherein the sensor detects analyte selected from the group consisting of carbohydrates, glycoproteins, glycopeptides, enzymes, glycolipids, hormones, lipoproteins, antibodies, antigens, haptens, steroids, theophylline, creatinine, drugs, polynucleotides, pesticides, and combinations thereof.

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23.(Currently Amended) The system of claim [1] 30, wherein the sensor detects glucose.

24.(Currently Amended) The system of claim [1] 30, wherein at least one of the excitation source, the first detector and the second detector are located on at least one semiconductor wafer.

25.(Currently Amended) The system of claim [1] 30, wherein the first and second detectors are adapted to simultaneously detect light received from the sensor.

26.(Currently Amended) The system of claim [1] 30, further comprising a means for pulsing the light emitted by the excitation source.

27.(Original) The system of claim 26, further comprising a means for phase locking the counting of signals at the detectors with the pulse emitted by the light pulsing means.

28.(Currently Amended) The system of claim [1] 30, further comprising a pump adapted to draw fluid from an individual for contact with the sensor.

29.(Original) The system of claim 28, wherein the fluid comprises interstitial fluid or blood.

30.(Original) A system for detecting an analyte, the system comprising:
a sensor adapted to detect the analyte, the sensor comprising a polymer matrix, fluorophores, and a membrane;
an excitation source to excite a fluorophore of the sensor;
a first detector adapted to detect light of a first wavelength emitted by the sensor;

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a second detector adapted to detect light of a second wavelength emitted by the sensor;

a third detector adapted to detect light of a third wavelength; and

a processor for processing signals corresponding to light detected by the detectors and for determining a property of the analyte.

31.(Original) The system of claim 30, wherein the excitation source is adapted to transcutaneously excite a fluorophore in the sensor.

32.(Original) The system of claim 30, wherein the detectors are adapted to transcutaneously detect light emitted by the sensor.

33.(Original) The system of claim 30 further comprising a transmitter for transmitting signals corresponding to light detected by the detectors to a remote location.

34.(Original) The system of claim 30 further comprising at least one filter to filter light received by at least one of the detectors.

35.(Original) The system of claim 30 further comprising a dichromatic mirror positioned to reflect light emitted by the excitation source and to transmit light emitted by the sensor.

36.(Original) The system of claim 35, further comprising a second dichromatic mirror positioned to reflect a first portion of the light transmitted through the first dichromatic mirror and to transmit a second portion of the light transmitted through the first dichromatic mirror.

37.(Original) The system of claim 36, further comprising a third dichromatic mirror positioned to reflect a first portion of the light transmitted through the second dichromatic mirror and to transmit a second portion of the light transmitted through the second dichromatic mirror.

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38.(Original) The system of claim 30, further comprising a fiber optic operatively coupled to the excitation source.

39.(Original) The system of claim 30, further comprising a fiber optic operatively coupled to at least one of the detector to transmit light from the sensor to the at least one detector.

40.(Original) The system of claim 30, wherein the fiber optic comprises a bundle of optical fibers, a first portion of the fibers being operatively connected to the first detector, a second portion of the fibers being operatively connected to the second detector, and a third portion of the fibers being operatively connected to the third detector.

41.(Original) The system of claim 30, wherein the third detector is adapted to detect light emitted by skin when the skin is excited by the excitation source.

42.(Original) The system of claim 40, wherein the processor is programmed with code to correct for the light emitted and scattered by the skin.

43.(Original) The system of claim 30, wherein the processor is programmed with code to:

receive data corresponding to a first $I(\lambda_1)$, a second $I(\lambda_2)$, and a third $I(\lambda_B)$ intensity measured at a first (λ_1) , a second (λ_2) , and a third (λ_B) wavelength; the third wavelength (λ_B) being selected such that the intensity detected at the third wavelength (λ_B) consists of background intensity;

correct the intensity at the first wavelength $I(\lambda_1)$ based on the third fluorescence intensity $I(\lambda_B)$ and a first predetermined correction function $B(\lambda_1)$; and

correct the intensity at the second wavelength $I(\lambda_2)$ based on the third intensity $I(\lambda_B)$ and a second predetermined correction function $B(\lambda_2)$.

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44.(Original) The system of claim 43, wherein the processor further comprises code to calculate a ratio of the corrected intensity at the first wavelength (λ_1) to the corrected intensity at the second wavelength (λ_2).

45.(Original) The system of claim 43, wherein the processor further comprises code to determine a property of the analyte.

46.(Original) The system of claim 45, wherein the property is concentration.

47.(Original) The system of claim 30, wherein the processor is programmed with code to:

receive data corresponding to a first $I(\lambda_1)$, a second $I(\lambda_2)$, and a third $I(\lambda_3)$ intensity at a first λ_1 , a second λ_2 , and a third λ_3 wavelength, respectively;

correct the intensity at the first wavelength $I(\lambda_1)$ based on the intensity at the third wavelength $I(\lambda_3)$ and a first set of three predetermined correction functions $D(\lambda_1)$, $A(\lambda_1)$, $B(\lambda_1)$; and

correct the intensity at the second wavelength $I(\lambda_2)$ based on the intensity at the third wavelength $I(\lambda_3)$ and a second set of three predetermined correction functions $D(\lambda_2)$, $A(\lambda_2)$, $B(\lambda_2)$.

48.(Currently Amended) A method of determining the concentration of an analyte using the system of claim 30 [1], the method comprising
exciting a fluorophore located in the sensor,
detecting light of a first wavelength emitted by the sensor;
detecting light of a second wavelength emitted by the sensor, and
determining the concentration of the analyte based upon a corrected intensity of the light of the first wavelength and a corrected intensity of the light of the second wavelength.

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49.(Original) The method of claim 48, further comprising determining the ratio of the intensity of the light emitted by the sensor at the first wavelength to the intensity of the light emitted by the sensor at the second wavelength.

50.(Original) The method of claim 48 further comprising determining the excited state fluorescence lifetime of the light emitted by the sensor at at least one of the first wavelength and the second wavelength.

51.(Original) The method of claim 48, wherein the sensor is implanted and the exciting comprises transcutaneously exciting fluorophores of the implanted sensor.

52.(Original) The method of claim 48, wherein the sensor is implanted and the detecting comprises transcutaneously detecting fluorophores of the implanted sensor.

53.(Original) The method of claim 48 further comprising transmitting signals corresponding to the detected light to a remote location.

54.(Original) The method of claim 48 further comprising detecting light of a third wavelength.

55.(Original) The method of claim 48 further comprising
drawing fluid comprising the analyte from an individual; and
contacting the sensor with the fluid.

56.(Original) A device comprising a detector-emitter array for detecting an analyte, the detector-emitter array comprising:

an excitation source adapted to excite a fluorophore of a sensor
comprising fluorophores;
a first detector adapted to detect fluorescence light of a first wavelength
emitted by the sensor;

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a second detector adapted to detect fluorescence light of a second wavelength emitted by the sensor; and
a third detector adapted to detect light of a third wavelength.

57.(Original) The device of claim 56, further comprising a transmitter for transmitting a signal corresponding to light detected by the detectors to a remote location.

58.(Original) The device of claim 56, wherein the excitation source is adapted to transcutaneously excite a fluorophore of the sensor.

59.(Original) The device of claim 56, wherein the detector is adapted to transcutaneously detect light emitted by the sensor.

60.(Original) The device of claim 56, further comprising a processor for processing signals generated by the detectors.

61.(Original) The device of claim 60, wherein the excitation source is positioned to provide excitation radiation to a first area of the sensor and the detectors are positioned to detect light emitted from the sensor at a second area of the sensor, the first area being in a spaced apart relation to the second area.

62.(Original) The device of claim 61, further comprising an amplifier and an A/D converter for amplifying and digitizing the signal from the first detector.

63.(Original) The device of claim 62, further comprising a clock for controlling a duration of a pulse emitted by the excitation source and for controlling acquisition of first data, second data, and third data from the first, second, and third detectors.

64.(Original) The device of claim 63 further comprising a transmitter for transmitting the first data, the second data, and the third data to a remote location.

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65.(Original) The device of claim 64 further comprising an additional processor for calculating a concentration of the analyte based on the first data, the second data, and the third data.

66.(Original) A system for detecting an analyte, the system comprising:
a sensor adapted to detect the analyte, the sensor comprising a polymer matrix, a membrane and fluorophores;
an excitation source to excite a fluorophore of the sensor;
a filter device for selecting from at least one of a first filter for filtering light of a first wavelength emitted by the sensor and a second filter for filtering light of a second wavelength emitted by the sensor;
a detector to detect light emitted by the sensor; and
a processor for processing signals corresponding to light detected by the detector.

67.(Original) The system of claim 66, wherein the filter device comprises a liquid crystal filter tunable to the first wavelength and the second wavelength.

68.(Original) A method of detecting fluorescence emitted by a sensor using the system of claim 66, the method comprising:
exciting fluorophores of the sensor;
detecting light of a first wavelength emitted by the sensor; and
subsequently detecting light of a second wavelength emitted by the sensor.

69.(Original) The method of claim 68, wherein the exciting comprises transcutaneously exciting fluorophores of the sensor.

70.(Original) The method of claim 68, wherein the detecting comprises transcutaneously detecting light emitted by the sensor.

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71.(Original) A method of correcting a measured fluorescence intensity, the method comprising:

- exciting a fluorophore of a sensor comprising fluorophores;
- measuring a first $I(\lambda_1)$, a second $I(\lambda_2)$, and a third $I(\lambda_3)$ intensity at a first λ_1 , a second λ_2 , and a third λ_3 wavelength, respectively;
- correcting the intensity at the first wavelength $I(\lambda_1)$ based on the intensity at the third wavelength $I(\lambda_3)$ and a first set of three predetermined correction functions $D(\lambda_1)$, $A(\lambda_1)$, $B(\lambda_1)$; and
- correcting the intensity at the second wavelength $I(\lambda_2)$ based on the intensity at the third wavelength $I(\lambda_3)$ and a second set of three predetermined correction functions $D(\lambda_2)$, $A(\lambda_2)$, $B(\lambda_2)$.

72.(Original) The method of claim 71, further comprising

- determining the fraction f_1 of the intensity due to emission by a first set of fluorescently labeled molecules D; and
- determining the fraction f_2 of the intensity due to emission by a second set of fluorescently labeled molecules A.

73.(Original) The method of claim 72, wherein the determining is based on a predetermined first $I_D(\lambda_1)$, $I_A(\lambda_1)$, $I_B(\lambda_1)$, second $I_D(\lambda_2)$, $I_A(\lambda_2)$, $I_B(\lambda_2)$, and third $I_D(\lambda_3)$, $I_A(\lambda_3)$, $I_B(\lambda_3)$ intensity of the first set of molecules D, the second set of molecules A, and the background B at each of the first (λ_1), the second (λ_2), and the third (λ_3) wavelengths, and the first $I(\lambda_1)$, second $I(\lambda_2)$, and third $I(\lambda_3)$ intensities normalized to the intensity at the third wavelength λ_3 .

74.(Original) The method of claim 71, wherein the determining is based on a first $D(\lambda_1)$, $A(\lambda_1)$, $B(\lambda_1)$, second $D(\lambda_2)$, $A(\lambda_2)$, $B(\lambda_2)$, and third $D(\lambda_3)$, $A(\lambda_3)$, $B(\lambda_3)$ predetermined correction coefficient related to the first set of molecules D, the second set of molecules A, and the background B at each of the first (λ_1), the second (λ_2), and the third (λ_3) wavelengths.

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75.(Original) The method of claim 71, wherein the determining comprises using the following equations:

$$f_1 = -\frac{-A(\lambda_3)*B(\lambda_2)+A(\lambda_2)B(\lambda_3)+A(\lambda_3)*I(\lambda_2)-B(\lambda_3)*I(\lambda_2)-A(\lambda_2)*I(\lambda_3)+B(\lambda_2)*I(\lambda_3)}{A(\lambda_3)*B(\lambda_2)-A(\lambda_2)B(\lambda_3)-A(\lambda_3)*D(\lambda_2)+B(\lambda_3)*D(\lambda_2)+A(\lambda_2)*D(\lambda_3)-B(\lambda_2)*D(\lambda_3)}$$

$$f_2 = -\frac{B(\lambda_3)*D(\lambda_2)-B(\lambda_2)D(\lambda_3)-B(\lambda_3)*I(\lambda_2)+D(\lambda_3)*I(\lambda_2)+B(\lambda_2)*I(\lambda_3)-D(\lambda_2)*I(\lambda_3)}{-A(\lambda_3)*B(\lambda_2)+A(\lambda_2)B(\lambda_3)+A(\lambda_3)*D(\lambda_2)-B(\lambda_3)*D(\lambda_2)-A(\lambda_2)*D(\lambda_3)+B(\lambda_2)*D(\lambda_3)}$$

76.(Original) A method of determining a property of an analyte in a fluid, the method comprising the method of claim 74 and further comprising calculating the ratio of the fluorescence intensity of the first set of molecules D to the fluorescence intensity of the second set of molecules A by dividing f_1 by f_2 .

77.(Original) A method of determining the ratio of the fluorescence intensity of an energy donor D to the fluorescence intensity of an energy acceptor A of a sensor, the method comprising the method of claim 71 wherein calculating the ratio of the donor fluorescence intensity to the acceptor fluorescence intensity is based on a first $D(\lambda_1)$, $A(\lambda_1)$, $B(\lambda_1)$, second $D(\lambda_2)$, $A(\lambda_2)$, $B(\lambda_2)$, and third $D(\lambda_3)$, $A(\lambda_3)$, $B(\lambda_3)$ predetermined fluorescence coefficient of the donor D, the acceptor A, and the background B at each of first (λ_1), the second (λ_2), and the third (λ_3) wavelengths and the first $I(\lambda_1)$, second $I(\lambda_2)$, and third $I(\lambda_3)$ intensities normalized to the third $I(\lambda_3)$ intensity.

78.(Original) The method of claim 77, wherein D is the donor fluorescence intensity due to direct excitation and A is the acceptor fluorescence intensity due to energy transfer.

79.(Original) A method of correcting for fluorescence intensity associated with a background component, the method comprising:

exciting a sensor comprising fluorophores;

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measuring a first $I(\lambda_1)$, a second $I(\lambda_2)$, and a third intensity $I(\lambda_B)$ corresponding to emission of the sensor at a first (λ_1), second (λ_2), and third wavelength (λ_B), the third wavelength (λ_B) being selected such that the intensity detected at the third wavelength (λ_B) consists of background signal;

correcting the intensity at the first wavelength $I(\lambda_1)$ based on the third intensity $I(\lambda_B)$ and a first predetermined correction function $B(\lambda_1)$; and

correcting the fluorescence intensity at the second wavelength $I(\lambda_2)$ based on the third fluorescence intensity $I(\lambda_B)$ and a second predetermined correction function $B(\lambda_2)$.

80.(Original) A method of determining a property of an analyte, the method comprising the method of claim 79 and further comprising calculating the ratio of the corrected intensity at the first wavelength (λ_1) to the corrected intensity at the second wavelength (λ_2).

81.(Original) The method of claim 80, wherein the property is the concentration of the analyte.

82.(Original) The method of claim 80, wherein the background signal is due to skin.

83.(Original) The method of claim 80, wherein the first wavelength is 600 nm, the second wavelength is 700 nm, and the third wavelength is 565 nm.

Please add the following new claims.

84.(New) The system of claim 30, wherein said excitation source comprises a light emitting diode.

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85.(New) The system of claim 84 further comprising a filter positioned to filter light emitted by the excitation source.

86.(New) The system of claim 30 further comprising a filter positioned to filter light emitted by the excitation source.

87.(New) The system of claim 30 further comprising a partially reflecting mirror for reflecting a first portion of light emitted by said excitation source and transmitting a second portion of light emitted by said excitation source.

88.(New) The system of claim 84 further comprising a partially reflecting mirror for reflecting a first portion of light emitted by said excitation source and transmitting a second portion of light emitted by said excitation source.

89.(New) The system of claim 30, wherein the detectors are in the form of a detector array.

90.(New) The system of claim 89, wherein the detector array comprises at least one of a photodiode array and a charge coupled array.